Manufacture of Tocopheryl Acetate

The present invention relates to a novel process for the manufacture of tocopheryl acetate and novel intermediates used therein. (All-rac)-α-tocopherol itself is known to be the most active industrially important member of the vitamin E group.

Industrial syntheses of vitamin E (α-tocopherol) are based on the reaction of 2,3,5-trimethylhydroquinone with isophytol, phytol or a phytyl halide: see Ullmann's Encyclopedia of Industrial Chemistry Vol. A27, VCH (1996), pp. 478-488. Since α-tocopherol is labile under oxidative conditions, it is usually converted into its acetate which is more stable and more convenient to handle. Thus, the manufacture of the usual commercial form of vitamin E, viz. tocopheryl acetate, involves the additional step of esterifying α-tocopherol (as obtained by the acid-catalysed reaction of 2,3,5-trimethylhydroquinone with isophytol, phytol or a phytyl compound, e.g. a halide). In turn, 2,3,5-trimethylhydroquinone is usually obtained from ketoisophorone via 2,3,5-trimethylhydroquinone diacetate and saponification of the latter.

The present invention provides a new approach to the manufacture of tocopheryl acetate. According to this new approach, 2,3,6-trimethylhydroquinone-1-acetate is reacted with either isophytol or phytol to produce 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, or with a phytyl halide to produce 4-O-phytyl-2,3,6-trimethylhydroquinone-1-acetate which is then submitted to a rearrangement reaction to produce 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate and, finally, the 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate is submitted to a ring closure reaction to obtain tocopheryl acetate. The new approach is shown in the following Reaction Scheme wherein R denotes the remaining portion of the isophytol or phytyl halide molecule 2 or 3, respectively, i.e. 3,7,11-